A COMPARATIVE STUDY BETWEEN FIRST GENERATION AND SECOND GENERATION ANTIPSYCHOTICS OVER THE DEVELOPMENT OF METABOLIC SYNDROME IN PERSONS WITH FIRST EPISODE DRUG NAÏVE SCHIZOPHRENIA

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CERTIFICATE

This is to certify that this dissertation entitled **"A COMPARATIVE STUDY BETWEEN FIRST GENERATION AND SECOND GENERATION ANTIPSYCHOTICS OVER THE DEVELOPMENT OF METABOLIC SYNDROME IN PERSONS WITH FIRST EPISODE DRUG NAÏVE SCHIZOPHRENIA"** is the bonafide original work of **Dr. M.SURIYA MOORTHI**, in partial fulfilment of the requirements for **MD (Branch XVIII) Psychiatry** degree examination of THE TAMIL NADU DR. MGR MEDICAL UNIVERSITY to be held in April 2012.

Under the Guidance of
Prof.Dr.R.KUMAR, M.D., D.P.M.,
Director Institute of Mental Health,
Madras Medical College,
Chennai – 600 010.

Dr.V.KANAGASABAI, M.D.,
Dean
Madras Medical College & Rajiv Gandhi
Government General Hospital,
Chennai -600 003

DECLARATION

I, Dr.M.SURIYA MOORTHI, solemnly declare that this dissertation entitled, **"A COMPARATIVE STUDY BETWEEN FIRST GENERATION AND SECOND GENERATION ANTIPSYCHOTICS OVER THE DEVELOPMENT OF METABOLIC SYNDROME IN PERSONS WITH FIRST EPISODE DRUG NAÏVE SCHIZOPHRENIA"** is a bonafide work done by me, at Institute Mental Health, Madras Medical College, Chennai – 600 010, during April 2011 to November 2011 under the guidance and supervision of **Prof.Dr.R.KUMAR, M.D., D.P.M**., Director, Institute of Mental Health, Madras Medical College, Chennai - 600 010.

The dissertation is submitted to the Tamilnadu Dr.M.G.R. Medical University, towards partial fulfillment of the regulations for the award of degree of MD (Branch XVIII) Psychiatry.

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CONTENTS

INTRODUCTION

Schizophrenia is a variable, significant and disruptive psychopathology, affecting every aspect of human life experiences like perception, cognition, emotion and behaviour, resulting in profound and often long lasting impairment, not only for persons affected, but also for the family and society, causing huge consumption of health costs, distress, loss of manpower, quality of life and productivity and 'arguably the worst disease affecting mankind, even AIDS not exempted' [Nature 1988].

It has puzzled physicians, philosophers and general public alike for centuries, as if it is a single disease, but it is probably comprises a group of syndromes due to multifactorial aetiology involving genetic, developmental, psychoneuroimmunological and environmental interactions in manifesting the disease.

Schizophrenia affects approximately 1% of the population, involving all cultures, society, race and nations, and commonly affecting during the fertile period of adolescent and young adulthood with a tendency for chronic course.

The treatment of schizophrenia has evolved over a long period of history with ancient remedies of plant extracts,with the revolutionary introduction of chlorpromazine in the 1950's and the beginning of research on psychopharmacology. Based on the clinical improvement of psychotic

symptoms and molecular studies of neurotransmitters and receptors,the dopaminergic hypothesis of schizophrenia was proposed for these early indroduction of psychotropic drugs, following the indroduction of chlorpromazine, preferentially blocking dopamine 2 receptors, hence these drugs were called dopamine antagonists or typical or first generations antipsychotics.

Apart from the effectiveness, it caused movement disorders of both acute and chronic [Tardive dyskinesias] in addition to other side effects, prompting research for drugs with minimum side effect profile resulting in the introduction of Dopamine-serotonin antagonists or atypical or second generation [preferentially blocking serotonin receptors] antipsychotics with different side effect profiles and equal efficacy except clozapine with much enthusiasm. [Canadian journal of psychiatry 2005;50;703-14.]

Although they were associated with less incidence of dyskinesias, soon it was found that they cause various derangements in metabolic parameters like weight gain, hypertension, dyslipidemia and dysregulation of glucose metabolism, which are established risk factors for cardiac and cerebrovascular complications, which causes catastrophic implications and premature death, requiring long term prophylaxis, dispelling the myth of superiority of atypicals over the typical antipsychotics. [schizophrenia Research 2004;71;195-212].

So the rational of the study is to find out the emergence of metabolic syndrome, which was established in various studies in the past, of the second generation antipsychotics and comparing it against first generation antipsychotics, in individuals with drug naïve first episode of schizophrenia to avoid the disease effect, in our Institute of mental health, Madras Medical College, Chennai-10.

REVIEW OF LITERATURE

METABOLIC SYNDROME

It is, relatively a new concept involving multiple systems resulting in long lasting morbidity and mortality. It can be defined as a constellation of lipid and non-lipid risk factors of metabolic origin, closely related to each other via insulin resistance. It includes obesity, atherogenic dyslipidemia, elevated blood pressure [with or without glucose intolerance], prothrombotic and proinflammatory states. **[Pi sunyer FX ;Metabolic syndrome. Med clinic North America 2007' 91;1020-40].**

PATHOGENESIS

The pathogenesis of metabolic syndrome is complex and the interactions between the individual components are poorly understood as 1.Complex interaction between visceral adipose tissue and insulin resistance is widely accepted 2.Visceral obesity is atherogenic due to lipolysis and release non-esterified free fatty acids.3.Increased hepatic and plasma free fatty acids causes glucose dysregulation and vasoconstriction resulting in elevated blood pressure.4.Other by-products of lipolysis like pro-inflammatory markers, damaging vascular system include angiotensinogen, adipsin, adiponectin, leptin, interleukin-6, and tumour necrosis factor- **[Fernandez Real and Ricart 2003, Sutherland et al 2004, Weisberg et al 2003].** According toMc envoy, in psychiatric populations, the clinical antipsychotic trial of intervention

effectiveness schizophrenia trial [CATIE] shows 40.9 percent [male-36, female-51.6]. And in bipolar affective disorder it is 30 percent using the NCEP-ATP III criteria- Fagiolini et al. 2005. Schizophrenia has 2.5 times higher risk of cardio and cerebrovascular deaths- **[Arch Gen Psychiatry 2007;64'242-49].**

PHARMACOLOGICAL MANAGEMENT OF SCHIZOPHRENIA

Apart from the psychosocial management of schizophrenia as a part of the holistic approach, Current evidence based pharmacotherapeutics play an important role and it can be broadly divided in to two groups based on the structures and clinical profile.

FIRST GENERATION ANTIPSYCHOTICS.

They represent the first group of effective agents introduced in the 1950's and thereafter, with dopamine -2 receptor antagonism, causing acute and chronic neurological side effects at their clinically effective doses. clinically it can be divided in to low potency drugs [phenothiazines] having significant alpha blocking and ant cholinergic actions and less propensity to cause EPS, and middle and high potency with less alpha blocking, anticholinergic and sedation. Eg. Haloperidol, a potent buterophenone derivative, is the representative drug with a potent D2 blocker with minimal anticholinergic and autonomic effects prone to increased occurrence of neurological [movement disorders] side effects.

SECOND GENERATION ANTIPSYCHOTICS.

These came in to clinical use in the 1970's with low affinity for dopamine 2 receptor, greater affinities for serotonin 1A, 2A, 2C, 367 nor-epinephrine and histamine receptors with less neurological side effects, but greater propensity for metabolic side effects, called atypical/serotonin-dopamine antagonist without superior efficacy than typical or with limited edge except clozapine. Risperidone is one of the commonly used drugs in Indian settings, which has potent antagonism at D2 receptor, 5HT-2A and also high affinity for Alfa -1 and 2, H1 receptor with moderate affinity for5HT-1C, 1D, 5HT-2A and weak affinity for D1 receptor with no affinity for adrenergic and cholinergic receptors.

ANTIPSYCHOTICS – EQUIVALENT DOSES

Antipsychotics vary greatly in potency and is expressed as differences in neuroleptic or chlorpromazine equivalents based on the early dopamine binding studies and some on largely by clinical experiences, for first generations and it is somewhat inappropriate for second generations due to their usually well defined dose-response relationship, though it is still followed in comparative studies.

EQUIVALENT DOSES IN mg/DAY [FOR 100mg OF CHLORPROMAZINE/DAY].

Fluphenazine-2

Trifluoperazine-5

Flupentixol-3

Zuclopenthixol- 5

Haloperidol 3, Maudslay guidelines 9th edition.

Sulpride-200

Pimozide-2

Loxapine-10

Resperidone-2

Olanzapine-5

Quetiapine-75

Ziprazidone-60

Aripiprazole 7.5 - **[J Clin Psychiatry 2003;64;663-7]**

DRUG EMERGENT METABOLIC SYNDROME OBESITY

Obesity is a chronic illness due to excess body fat by enlargement of fat cell size [hypertrophic] or increase in fat cell number [hyper plastic] or both and results from greater caloric intake than expenditure.Women typically collect fat in gluteofemoral region giving the ‘pear shape’ called gynoid or peripheral obesity.Men collects fat usually in the abdomen both subcutaneous and visceral region giving the ‘Apple shape’ called android /upper body/central obesity which is more associated with CAD health. Obesity is assessed by Body Mass Index [BMI].

OBESITY AND ANTIPSYCHOTICS

Weight gain liabilities is to be considered holistically in terms of sociodemographics, dietary habits, co morbidities like binge eating, hypothyroidism and other medical illnesses likely to be associated to the metabolic derangements, patient behaviour like smoking and inactivity, family history, premorbid weight status, body composition, psychiatric illnesses and treatment factors.A weight gain liability of both first generation and second generation was reported based on the meta-analysis of 81 studies in schizophrenia in short time (10 weeks) for clozapine 4kg, olanzapine 3.5kg, chlorpromazine 2.1kg, Risperidone 2kg and ziprasidone .04kgmg.- **Am J Psychiatry 156;1686-96, 1999.**

An increase which is more than 7% of the baseline weight for olanzapine 10 times, quitiapine 4 times, risperidone 2 times was reported – **casey et al 2004.** The rate is more during the first 2-3 months, but continuous effect reported for clozapine even after1 year and 6-9 months for olanzapine and some had continuous rise for several years.The pattern of increase is more in the form of subcutaneous and intra abdominal fat deposition. – **(zhang et al 2004.**

Weight gain correlation studies.1.Younger age more risk -Kelly et al 1998, lane et al 2003. 2.Female more risk - Gopalaswamy and morgan 1985. 3.Males more risk - Kinon et al 1998. 4.No sex difference- -Lane et al 2003. 5.Ethnicity-non whites more risk - Bassoon et al 2001,lane et al 2003. 6.Cigarette smoking-no association - Ellingrod et al 2002. 6.Normal or underweight more risk- Kinon et al 1998,lane et al 2003. 7.Antipsychotic naive more risk-Wetterling and mussigbrodt 1999. 8.Positive association for dose-Lane et al 2003, nemerof 1997. 9.No association for dose - Ganguly 1999, Johnson and breen 1979. 10.Duration of rise -3.3 kg for risperidone after 1 year by Amry et al 1997 and after 2 years- Csernansky et al 1999 11.Positive relation with Clinical response -Bustillo et al 2003,dobmeir et al 2000kinon et al 1998. 12.No correlation -Lamberti et al1992, umbricht et al 1994. 13.Positive relation with olanzapine and clozapine and no relationship with risperidone and haloperidol -Zang et al 2003. 14.Atypical more than conventional - comprehensive review by ewcomer 2005.

Obese persons have down regulations of striatal D2 receptors and increased feeding behaviour. –wang et al 2001. Serotonin is a satiety factor influencing food preferences -De vry and schrieber 2000.Histamine 1,2,3 receptors play in the regulation of body weight, drinking and feeding behaviour with H1 receptor showing high correlation for short term increases. GABAnergic medications promote weight gain and glutamate agonists stimulate feeding behaviour. Prolactine stimulates food intake, fat deposition, and lipolysis and deceases insulin binding and glucose uptake in adipocytes.Leptin is an adipocyte-derived peptide that regulates energy intake, energy expenditure. Ghrelin is a 28-amino acid orexigenic peptide and is inversely associated with energy balance.Patients receiving antipsychotic medication frequently report a change in the subjective feeling of fullness and satiety, food preferences- (Theisen et al. 2003). Dysregulation of central mechanisms (e.g., hypothalamic) also seen. Uncoupling proteins occupy a pivotal role in regulating energy expenditure through peripheral mechanisms.

DIABETES MELLITUS

- Type I DM- Characterised by no or limited insulin, seen in early life and accounts for 5 to 10 percent of all diabetes. It is predominantly T cell mediated auto immune process selectively destroys insulin producing pancreatic beta cells.

- Type II - usually due to insulin resistance, later on insulin deficiency may occur.

Genetic vulnerability with obesity are common causes, leading to many complications like cardiac diseases, stroke, kidney diseases ,peripheral vascular diseases, retinopathy, leg ulcers and amputations ,neuropathy, digestive diseases and periodontal disease In general, increase in insulin resistance is anticipated to occur secondary to increases in adiposity et al. - **(Ebenbichler 2003; Eder et al. 2001)**. A Significant minority of patients may experience glucose dysregulation independent of weight or adiposity differences- **Kemner et al. 2002; Koller and Doraiswamy 2002;**

The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study is a major ongoing National Institute of Mental Health-sponsored prospective trial designed to assess the efficacy of the second-generation antipsychotic agents olanzapine, quetiapine, risperidone, and ziprasidone, with perphenazine included as a representative first-generation agent. 1,493 patients with schizophrenia at 57 sites in the United States. The primary outcome measure is time to all-cause discontinuation. Phase I results were published in September 2005. olanzapine group gained more weight than patients in any other group (mean weight gain = 2lb per month), and 30% of patients in the olanzapine group gained 7% or more of their baseline body weight (vs. 7%-16% in the other groups; $P<0.001$). Olanzapine – treated patients also showed the greatest increases in total cholesterol (mean increase = 9.7 + 2.1 mg/dl),

with statistically significant differences between treatment groups in each of these indices- **(Lieberman et al. 2005)**.

DYSLIPIDEMIA

Induction of hyperlipidemia during antipsychotic therapy thus represents a serious condition not only because of its inherent impact on cardiovascular risk but also because it is occurring in a group that possesses considerable risk - (Saari et al. 2004).The atypical antipsychotics have a decreased liability for neurological side effects, but have a marked propensity for adverse metabolic outcomes, especially hyperlipidemia.- (Meyer and Koro 2004). This is bolstered by the recent publication of the double-blind, controlled data from Phases I and II of the CATIE Schizophrenia Trial- (Lieberman et al. 2005; Stroup et al. 2006).Typical antipsychotics , chlorpromazine and other low-potency phenothiazines, have greater effects on triglyceride concentrations.- **(Clark and Johnson 1960; Clark et al. 1967; Mefferd et al. 1958**

HYPERTENSION

It is a chronic, often symptomless condition defined arbitrarily as elevated blood pressure of 140/90 or more, most common form is idiopathic causing increased risk of CAHD, CVD and stroke, cardiomyopathy, renal failure, peripheral vascular disease

AETIOLOGY

- 90 percent are idiopathic but genetic and familial influences are seen.
- Pathophysiologically, activation of sympathetic nervous system and rennin angiotensin are important determinants.
- Transient regulation is by vasoconstriction of the smooth muscle media layer of the vessel walls of small arterioles and long term regulation is by renal excretion of sodium, potassium and free water.

SUMMARY OF SELECTED STUDIES

Reynolds et al. 2002	Chlorpromazine (69) Risperidone (46) Clozapine (4) Fluphenazine (3) Sulpiride (1)	123	Schizophrenia (DSM-IV)	Study	Treatment	Sample size (N)	Diagnosis
Zhang et al. 2003	Antipsychotics	117	First-episode Schizophrenia	Han Chinese	10 weeks	TaqIA polymorphism of dopamine D2 receptor gene (DRD2)	Non significant
Templeman et al. 2005	Risperidone (26) Olanzapine (19) Haloperidol (10) Quetiapine (11) Ziprasidone (6) Amisulpiride (1)	73	First-episode psychosis	Spanish Caucasian	6weeks, 3 months, 9 months	5-HT2c gene (-759C/T) and leptin (-2548A/G)	Less weight gain with -759T variant allele; significant association between -2548 leptin polymorphism and antipsychotic induced weight gain at 6 weeks or 3 months.
Muller et al. 2005	Olanzapine (21) Risperidone (13) Haloperidol (13) Clozapine (12)	59	Chronic Schizophrenia / schizoaffective (DSM-IV)	African American (33) Caucasian (15) Hispanic (8) Asian Pacific (2) American Indian (1)	14 weeks	SNAP-25 gene.	Mnl and Tai I associate with both clinical response (P=0.01 and P=0.03) and weight gain (P=0.01 and P =0.004) but not Dde I; Significant association with more weight gain in the T/T genotype of Mn/I (cf. T/G or G/G) and C/C genotype of Tail (cf. T/C or T/T)

METHODOLOGY

A COMPARATIVE STUDY BETWEEN FIRST GENERATION AND SECOND GENERATION ANTIPSYCHOTICS OVER THE DEVELOPMENT OF METABOLIC SYNDROME IN PERSONS WITH FIRST EPISODE DRUG NAÏVE SCHIZOPHRENIA

AIM

To compare the first generation and second generation antipsychotics in first episode schizophrenia.

OBJECTIVES

- To prospectively study the development of metabolic syndrome as per the AMERICAN HEART ASSOCIATION [Review of US national cholesterol education programme adult treatment panel III-2001] criteria between first and generation antipsychotics in drug naïve first episode schizophrenia.

- To study the impact of familial and premorbid metabolic profiles during the treatment.

HYPOTHESIS

Second generation antipsychotics cause more metabolic derangements than first generation antipsychotics.

NULL HYPOTHESIS

There is no difference between these two groups over the development of metabolic syndrome.

STUDY DESIGN

Prospective

Comparative

Randomized

6 months duration, recruitment period from April 1st to May 15th and the data collection was completed in November 15th.

CONSENT APPROVAL

Apart from history, both patient and informants were explained about the details of the study and the informed consent was obtained both from the patient and the informants in the prescribed format. The institutional ethical committee's approval was obtained prior to the study and the protocols were followed throughout the study.

STUDY CENTRE

Outpatient department, Institute mental health,Chennai-10

MATERIALS AND METHODS

INCLUTION CRITERIA

First episode schizophrenia as per DSM IV-TR.

AGE-18 TO 45 yrs.

Both sexes

EXCLUTION CRITERIA

Comorbid psychiatric illness.

Comorbid substance abuse.

Comorbid diabetes mellitus, hypertension, obesity, dyslipidemia.

Other medical illness.

PROCEDURE

All new persons attending out- patient department with the diagnosis of first episode drug naive schizophrenia as per DSM IV–TR diagnostic criteria from April 1st May15th were included. Total number of persons screened was 67. 11 persons were excluded due to the medical illness and substance abuses. 2 persons were not willing to enter the study and 1 person preferred to get follow-up at the local leval.The total number of individuals selected is 53.They

were divided in to two groups with 24 in haloperidol and 29 in the risperidone by simple random method. Any one drug in first generation or second generation group of antipsychotics was used with Chlorpromazine equivalent doses of minimum and maximum dose.Anticholinergic and benzoddiazepines were used if needed. Drugs were allotted by simple random method by the treating clinician. On day one complete psychiatric history along with physical examination, baseline assessment of anthropometric measures and rating scales was done. Hematological investigations were done within a week.

INSTRUMENTS USED

PSYCHOPATHOLOGY

1 DSM IV-TR -Diagnostic criteria for schizophrenia.

2 PANSS [Positive and negative symptoms scale].

3 Simpson Angus rating scale.

METABOLIC ASSESSMENT

1. AMERICAN HEART ASSOCIATION [Review of US national cholesterol education programme adult treatment panel III-2001] criteria for metabolic syndrome.

2. DIABETES MELLITUS Overnight fasting plasma glucose.

3. HYPERTENTION 10 Minutes after relaxation Sitting posture 3 recordings at 10 minutes interval of average readings.

4. OBESITY Height with light clothing in centimeters with standardized scale. Weight in kilograms. Waist circumference in centimeters-measured over the midpoint between the lowest margin of the costal cartilage and the highest point of the iliac crest. Hip circumference-at the level of the most prominent part of the ischium posteriorly. Weight –Hip ratio. Body Mass Index—weight in kilograms divided by meters2.

LIPID PROFILE

Triglycerides, High density cholesterol, Total cholesterol after 12 hours fasting state.

ASSESSMENT INTERVAL

Baseline - Anthropometric measurements, psychopathological assessment by rating scales and blood investigations.

* Every two months-Laboratory investigations in additions to anthropometric measurements.

DATA COLLECTION

* SOCIODEMOGRAPHIC DATA

Name, age, sex, education, marietal status, occupation, religion, language are collected.

* LIFE STYLE HISTORY

Sedentary

Moderate physical work

Strenuous work

* FAMILY HISTORY -in first degree relatives.

Diabetes

Hypertension

Dyslipidemia

Obesity

Lifestyle

Medical illness

Psychiatric illness

Substance use including smoking.

Treatment for any of the above conditions.

ROUTINE PHYSICAL EXAMINATIONS

- **CLINICAL**

Psychiatric and medical history.

General examinations.

Systemic examinations.

- **LABORATORY**

Urinalysis.

Basic blood investigations.

Other investigations accordingly.

TESTS USED

1. Students T test [paired].

2. Chi-square test.

3. General linear model analysis.

4. Multivariate repeat measures -pillai's trace, wilk's lambda, Hotelling's trace, Roy's largest root.

5. Adjustment for multiple comparisons; Bonferroni corrections.

RESULTS

The current study is a randomised, prospective, comparative one between risperidone and haloperidol.the samples were first episode drug naïve schizophrenia, divided into two groups by simple random method. Out of 53 persons irregular follow up was seen in 2 persons in each group and they were excluded in the overall analysis. Risperidone group had 29 patients and 24 patients in haloperidol.The mean age in risperidone was 30.48(SD-8.761) and 26.08(SD-6.717).After applying t test for equality of means and Levene's test for equality variances significant differences were found with p value of .044(df 50.739). The majority were female, 66.7% in haloperidol group and 58.6% in Risperidone group. After applying chi square test no significance existed between the groups. (P-0.377).

The majority of the people were unmarried (64.2%) as against married one. It is 62.5% in haloperidol group and 65.5% in risperidone group without significant inter group difference. (p-.523).

Socioeconomic status was classified into lower, middle and upper and majority were lower class (58.6%) without significant group differences. (p.835).

LIFE STYLE CHARACTERISTICS

Most of the persons were sedentary (66%) without significant inter group differences (p166).

POSITIVE FAMILY HISTORY OF METABOLIC CONDITIONS

18.9% of samples had positive family history without intergroup differences(p.074).

Simpson angus score-no significant group difference (p.638).

Drug profile of both groups were as follows and there is no much difference between both groups after calculating chlorpromazine equivalent doses in terms of mg of cumulative risperidone (risperidone 102mg and for haloperidol group 84mg). P.451-df.1

Illness duration was classified into less than one year and more than one year. After applying chi square test no significant variation was found between both groups.(P.131).

Baseline parameters without intergroup differences with two tailed t test with equal variance assumed and not assumed with 95% CI).

	DRUG_CODE	N	Mean	Std. Deviation	Std. Error Mean	Significance (2 tailed)	Df
Age	HPL	24	26.08	6.717	1.371	.049	51
	R	29	30.48	8.761	1.627	.44	50.739
PANSS	HPL	24	117.75	30.805	6.288	.759	51
	R	29	120.55	34.547	6.415	.756	50.688
Height	HPL	24	160.29	7.086	1.446	.155	51
	R	29	157.21	8.248	1.532	.149	50.914
Weight	HPL	24	54.38	7.912	1.615	.569	51
	R	29	55.62	7.853	1.458	.570	49.026
Waist	HPL	24	81.69	5.532	1.129	.348	51
	R	29	83.29	6.557	1.218	.340	50.973
Hip	HPL	24	91.19	7.109	1.451	.496	51
	R	29	92.41	5.925	1.100	.504	44.866
BMI	HPL	24	21.3733	4.07488	.83178	.232	51
	R	29	22.6747	3.75449	.69719	.236	47.437
HDL	HPL	24	50.08	4.373	.893	.209	51
	R	29	48.48	4.710	.875	.206	50.289
Triglycerides	HPL	24	134.12	10.868	2.218	.602	51
	R	29	132.45	12.155	2.257	.599	50.667

BP_Sys	HPL	24	111.75	12.386	2.528	.600	51
	R	29	110.00	11.702	2.173	.602	48.010
BP_DIA	HPL	24	71.83	7.889	1.610	.667	50
	R	28	70.71	10.360	1.958	.661	49.366
Sugar_FAS	HPL	24	90.92	5.492	1.121	.512	51
	R	29	89.83	6.359	1.181	.507	50.890
Sug_pp	HPL	24	125.75	10.113	2.064	.282	51
	R	29	122.69	10.282	1.909	.282	49.454

At the end of two months the dependentant variables were assessed.Increases in weight, triglycerides, HDL cholesterol, fasting blood sugar, body mass index were more prominent with highly significant p value(p.002 for HDL, p .018 for PANSS reduction, p .000 for weight, triglycerides, blood sugar)

Between-Subjects Effects-BLOOD PRESSURE		
Source	df	Sig.
Intercept	1	.000
DRUG_CODE	1	.000
Error	47	

There was a significant differences was found in blood pressure of both systolic and diastolic with highly significant p value of .000, which is not found in anyother parameters. The mean fall is 3.2 systolic and 2.6 in diastolic for risperidone, and mean rise of 4 in systolic and 2.1 in diastolic for haloperidol.

At the end of four months BP_Sys4	HPL	122.27	15.920	49	.003
	R	110.31	11.361	36.298	.005
BP_dys4	HPL	79.36	8.471	49	.004
	R	72.21	8.407	45.183	.004

The same pattern of significant difference as in two months was continued in blood pressure changes between risperidone (p .004) and haloperidol (.003).

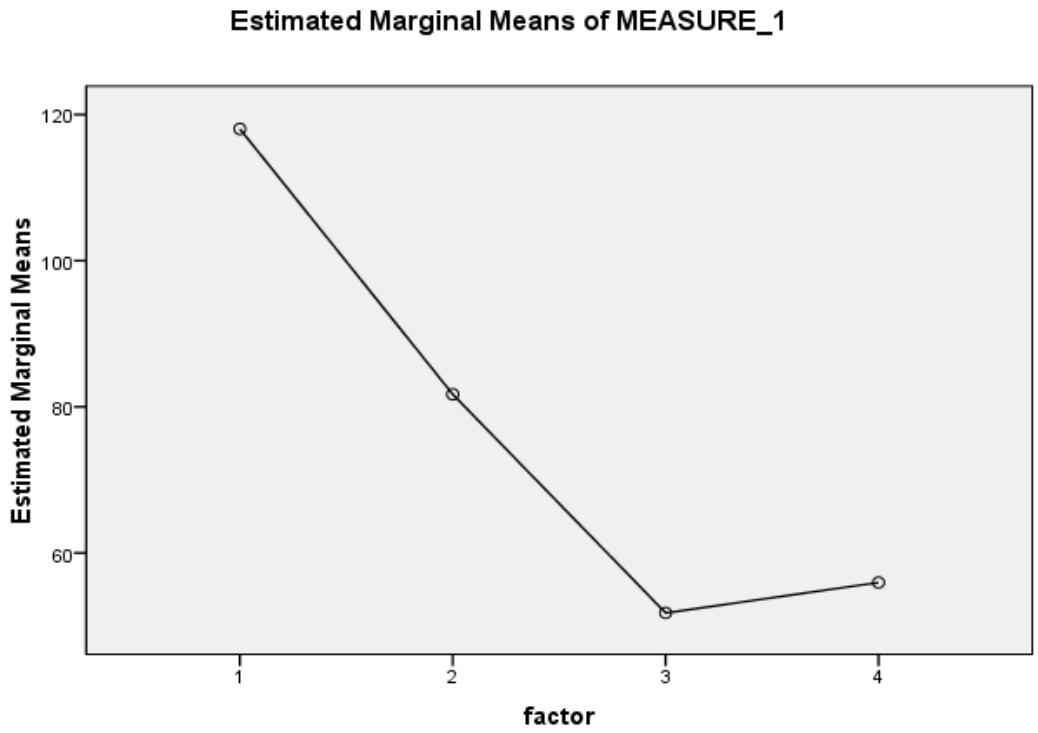
At the end of six months the inter group differences were more marked with p value of .000 for systolic and p value of .004 in risperidone and .005 in haloperidol.

BP_sys6	HPL	23	121.22	10.596	2.209	50	.000
	R	29	108.28	11.145	2.070	48.317	.000
BP_dia6	HPL	24	78.25	7.537	1.538	51	.005
	R	29	71.17	9.614	1.785	50.873	.004

Multi variate analysis was done to compare the marginal means of the two groups based on the linearly independent pair wise comparisons with pillais trace, wilks lambda,hotellings trace, roys largest root.adustment for multiple comparisons were done with bonferroni correction.Al values are with 95% CI.and p value sfgnificant below .05

PAIRWISE COMPARISONS OF PANSS SCORE

(I) factor	(J) factor	Mean Difference (I-J)	Std. Error	Sig.[a]
1	2	36.324*	2.789	.000
	3	66.255*	4.019	.000
	4	62.096*	3.890	.018
2	1	-36.324*	2.789	.000
	3	29.930*	2.595	.000
	4	25.772*	2.709	.018
3	1	-66.255*	4.019	.000
	2	-29.930*	2.595	.000
	4	-4.158	3.063	1.000
4	1	-62.096*	3.890	.018
	2	-25.772*	2.709	.000
	3	4.158	3.063	1.000



Reduction in PANSS score is significant from baseline to second months and from second month to fourth month.(p .018). Tests of Between-Subjects Effects The group difference is insignificant.(p.888). Rapid fall in PANSS occurred almost 40 points reduction in first two months.

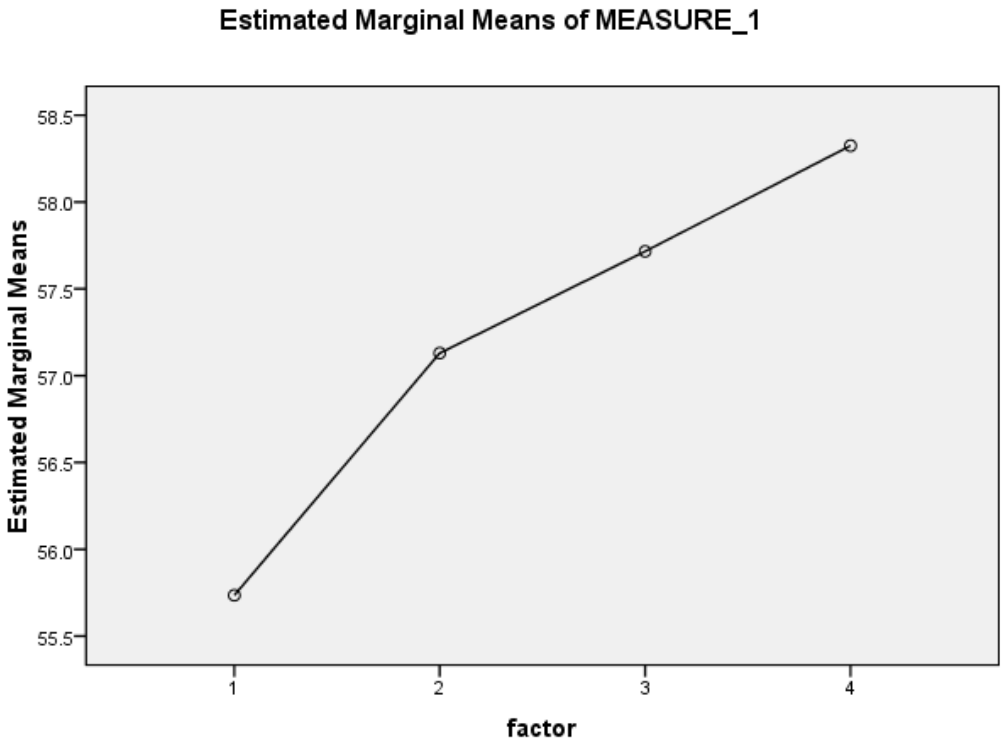
WEIGHT GAIN

All persons in the risperidone group developed weight gain and 20 persons (83.3%) in the haloperidol group with highly significant p value of .000 and no difference between groups(p value .505).

PAIRWISE COMPARISONS

Weight			Std. Error	Sig.[a]
(I) factor	(J) factor	Mean Difference (I-J)		
1	2	-1.394*	.172	.000
	3	-1.981*	.294	.000
	4	-2.589*	.383	.000
2	1	1.394*	.172	.000
	3	-.586	.249	.137
	4	-1.194*	.324	.004
3	1	1.981*	.294	.000
	2	.586	.249	.137
	4	-.608	.278	.203
4	1	2.589*	.383	.000
	2	1.194*	.324	.004
	3	.608	.278	.203

Source	df	Sig.
Intercept	1	.000
DRUG_CODE	1	.990
	47	



The graph shows rapid gain during the first 2 months (p .000)

BODY MASS INDEX

Weight gain is more marked in the first two months with a mean of 1.394 kg and less rise between 2 to 4 months. Tests of Between-Subjects Effects show less significant(p .990)

Significant change occurred as in weight gain with p value of .000 (95% CI) during the first two months.

PAIRWISE COMPARISONS

BMI-as in weight the most vulnerable period is first two months-p.000.

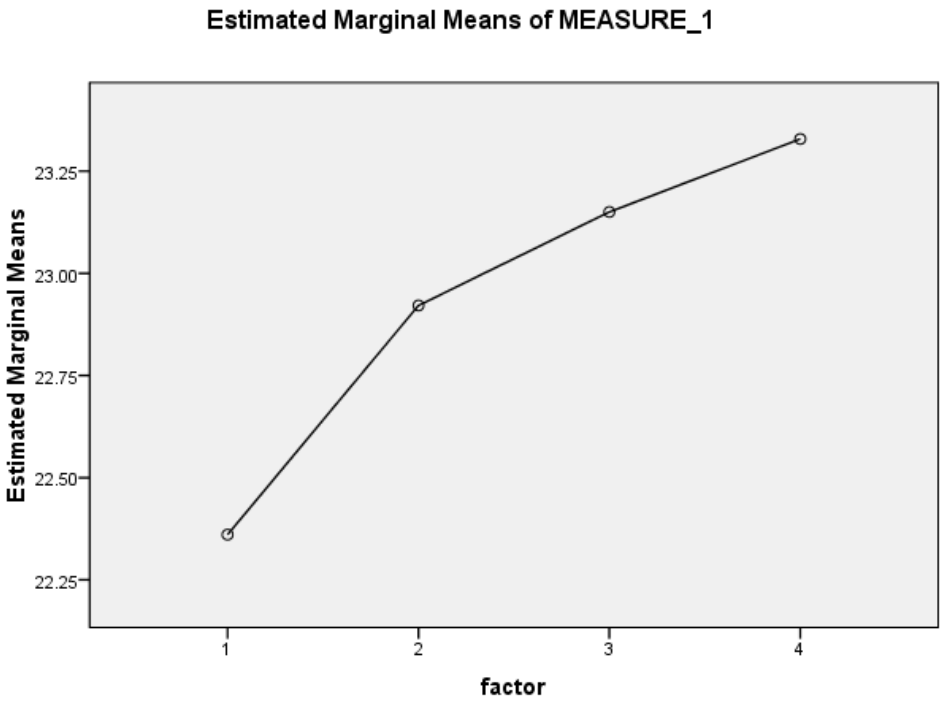
(I) factor	(J) factor	Mean Difference (I-J)	Std. Error	Sig.[a]
1	2	-.561*	.069	.000
	3	-.790*	.116	.000
	4	-.968*	.190	.000
2	1	.561*	.069	.000
	3	-.229	.096	.130
	4	-.408	.171	.126
3	1	.790*	.116	.000
	2	.229	.096	.130
	4	-.179	.141	1.000
4	1	.968*	.190	.000
	2	.408	.171	.126
	3	.179	.141	1.000

Tests of Between-Subjects Effects

Measure-BMI

Transformed Variable: Average

Source	**df**
Intercept	1
DRUG_CODE	1
The intergroup difference is insignificant-p value is .499 as in the graph	47



More rise in BMI up to 0.65 (P .000)

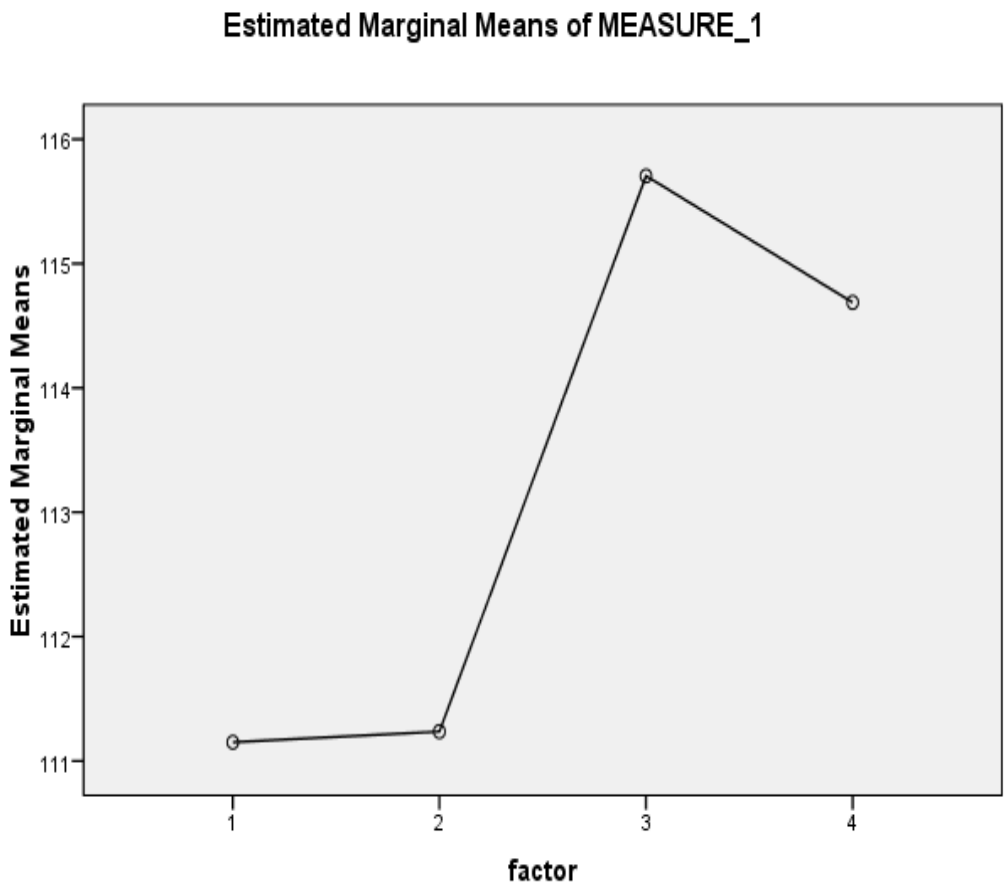
Blood pressure changes are less and it is more in risperidone group with p value of p.000 at 95% CI.

PAIRWISE COMPARISONS

Measure. Blood pressure

(I) factor	(J) factor	Mean Difference (I-J)	Std. Error	Sig.[a]
1	2	-.086	1.455	1.000
	3	-4.555	2.586	.508
	4	-3.538	1.481	.126
2	1	.086	1.455	1.000
	3	-4.469	2.406	.417
	4	-3.452	1.644	.247

Source	df	Sig.
Intercept	1	.000
DRUG_CODE	1	.000



The initial overall rise is confounded by fall in risperidone group. (p .000).

HDL cholestrol changes occurred in 19 persons(79.9%) in haloperidol group and in 26 persons(89.6%) in risperidone group. There are no differences between the groups (p .540).

PAIRWISE COMPARISONS

Measure:HDL

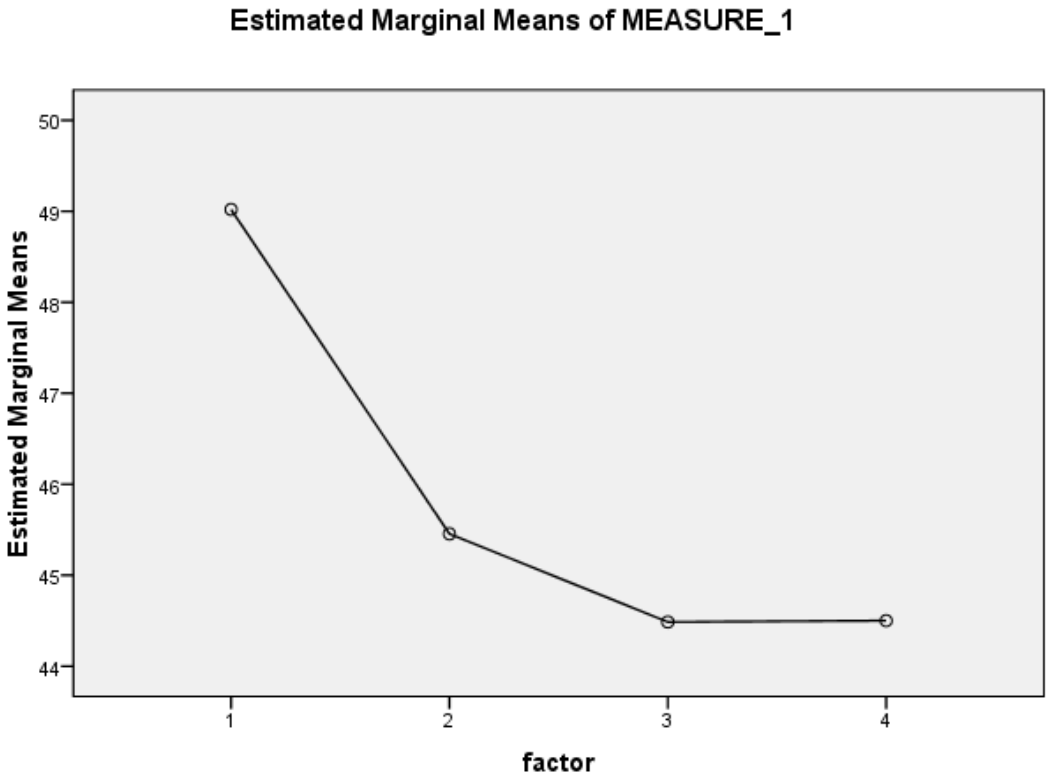
(I) factor	(J) factor	Mean Difference (I-J)	Std. Error	Sig.[a]
1	2	3.566*	.749	.000
	3	4.534*	.797	.000
	4	4.520*	.702	.000
2	1	-3.566*	.749	.000
	3	.969*	.247	.002
	4	.954*	.248	.002
3	1	-4.534*	.797	.000
	2	-.969*	.247	.002
	4	-.014	.305	1.000
4	1	-4.520*	.702	.000
	2	-.954*	.248	.002
	3	.014	.305	1.000

HDL decrease during the early period is highly significant (p .002)

Tests of Between-Subjects Effects

Source	df	Sig.
Intercept	1	.002
DRUG_CODE	1	.658
Inter group difference is insignificant.	43	

The HDL changes is less from 4th month to 6th month (p.858).



Hip circumference change seen 21 persons (87.5%) in haloperidol group and in all persons in resperidone group .it is more marked from 2nd month to 4th month (p .000) without group differences.

PAIRWISE COMPARISONS

Measure-HIP

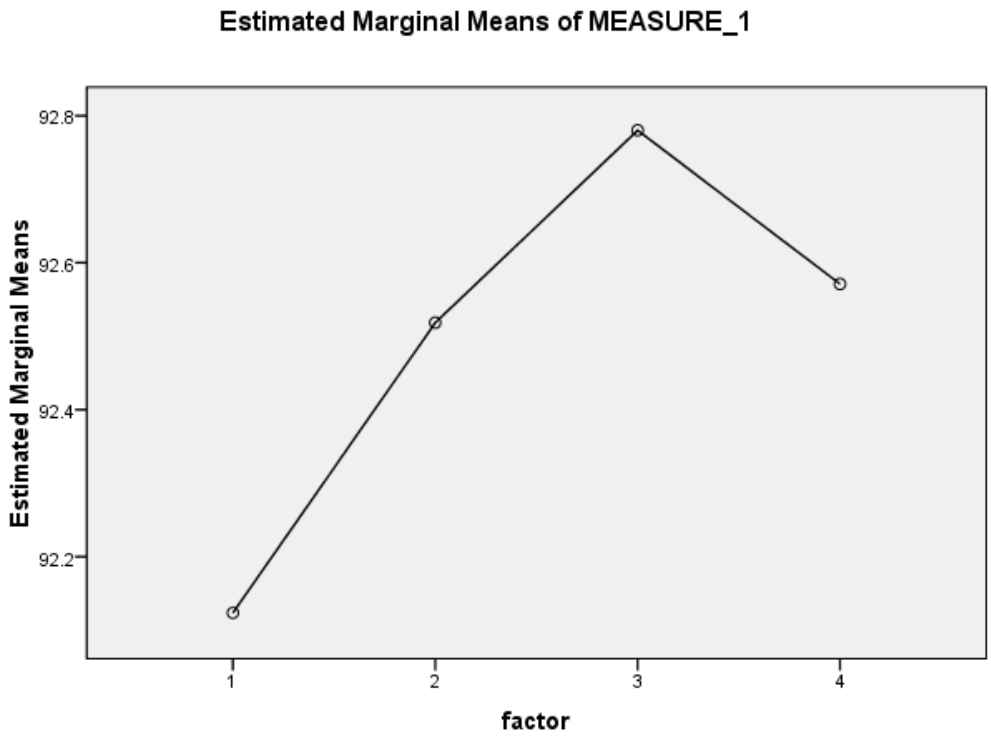
(I) factor	(J) factor	Mean Difference (I-J)	Std. Error	Sig.[a]
1	2	-.395	.386	1.000
	3	-.657	.412	.704
	4	-.447	.442	1.000
2	1	.395	.386	1.000
	3	-.262	.095	.051
	4	-.053	.184	1.000
3	1	.657	.412	.704
	2	.262	.095	.051
	4	.209	.200	1.000
4	1	.447	.442	1.000
	2	.053	.184	1.000
	3	-.209	.200	1.000

Tests of Between-Subjects Effects

Measure-HIP

Source	df	Sig.
Intercept	1	.000
DRUG_CODE	1	.561
There is no inter group differences	48	

Hip circumference rise is more up to 4 months (p .000) without inter group difference.



Increased triglyceride differences were seen in 19 persons (79.1%) and 25 persons (86.2%) in risperidone group, which is highly significant during the first two months.(p .012).

PAIRWISE COMPARISONS

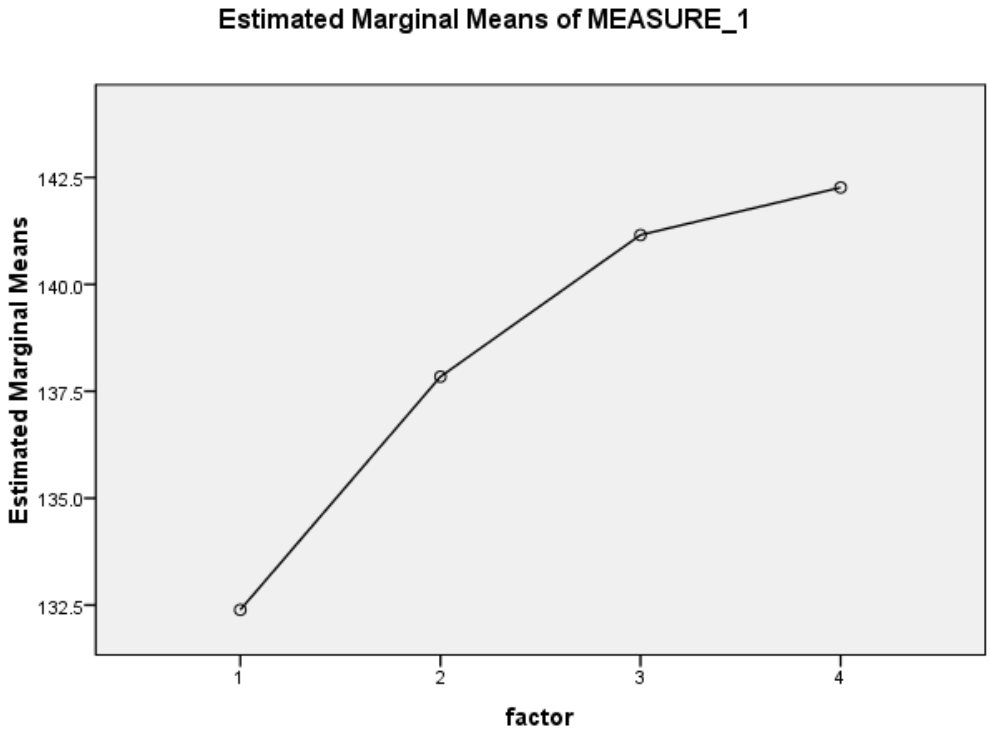
Measure: TRIGLYCERIDES

(I) factor	(J) factor	Mean Difference (I-J)	Std. Error	Sig.[a]
1	2	-5.454*	1.231	.000
	3	-8.766*	2.273	.002
	4	-9.877*	1.247	.000
2	1	5.454*	1.231	.000
	3	-3.313	2.116	.750
	4	-4.423*	1.337	.012
3	1	8.766*	2.273	.002
	2	3.313	2.116	.750
	4	-1.111	2.004	1.000
4	1	9.877*	1.247	.000
	2	4.423*	1.337	.012
	3	1.111	2.004	1.000

Source	Df	Sig.
Intercept	1	.000
DRUG_CODE	1	.652
Error	42	

Inter group difference is insignificant at p .652

Tests of Between-Subjects Effects



As seen in the graph 6 point rise seen in first 2 months (p .000) and less rise from 4th to 6th month.

PLASMA GLUCOSE

PAIRWISE COMPARISONS

Blood sugar[f] rise is more in the first two months with p value of .000 and .003

Measure-BLOOD SUGAR –fasting

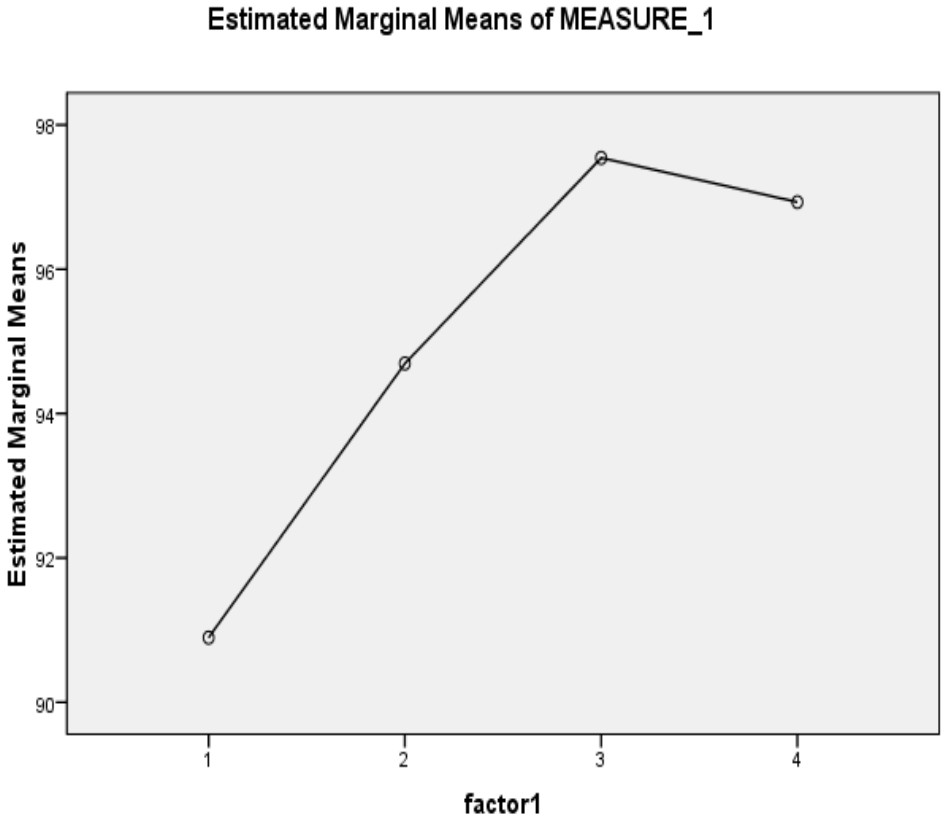
(I) factor1	(J) factor1	Mean Difference (I-J)	Std. Error	Sig.[a]
1	2	-3.799*	.999	.003
	3	-6.648*	1.495	.000
	4	-6.036*	1.028	.000
2	1	3.799*	.999	.003
	3	-2.849	1.305	.208
	4	-2.237	1.276	.522
3	1	6.648*	1.495	.000
	2	2.849	1.305	.208
	4	.613	1.414	1.000
4	1	6.036*	1.028	.000
	2	2.237	1.276	.522
	3	-.613	1.414	1.000

Tests of Between-Subjects Effects

Measure: Blood sugar

Transformed Variable: Average

Source	df	Sig.
Intercept	1	.000
DRUG_CODE	1	.587
No significance between the groups (p .587).	42	



Fasting sugar value rose up to 7 points in the first 4 months with p value of .000 waist circumference increases in waist circumferences were seen in 21 persons(87.5%) in haloperidol group and27persons (93.1%) in risperidone group with the p value of .005 995% CI). This is more marked during the first two months as seen in the graph.

PAIRWISE COMPARISONS

Measure: WAIST

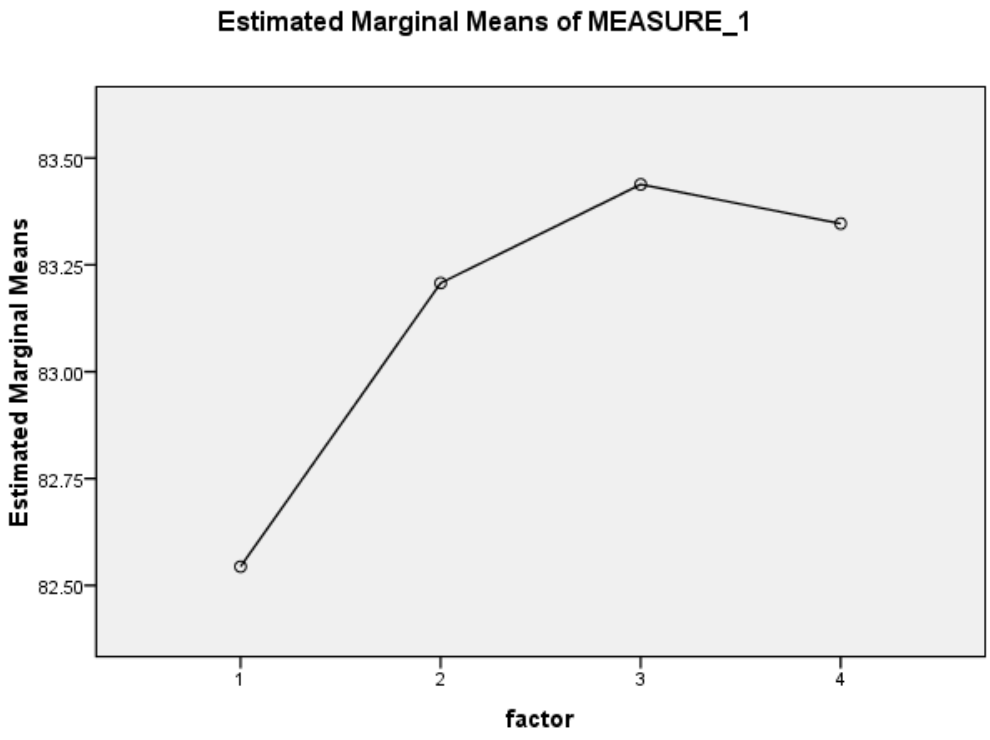
(I) factor	(J) factor	Mean Difference (I-J)	Std. Error	Sig.[a]
1	2	-.663	.475	1.000
	3	-.894	.468	.375
	4	-.803	.549	.902
2	1	.663	.475	1.000
	3	-.231*	.068	.008
	4	-.139	.267	1.000
3	1	.894	.468	.375
	2	.231*	.068	.008
	4	.092	.270	1.000
4	1	.803	.549	.902
	2	.139	.267	1.000
	3	-.092	.270	1.000

Tests of Between-Subjects Effects

Measure WAIST

Transformed Variable: Average

Source	Df	Sig.
Intercept	1	.000
DRUG_CODE	1	.246
Error	46	



DISCUSSION

Schizophrenia itself is a vulnerable one with at least two fold increased risk factor for the development of metabolic syndrome. Treatment with antipsychotics unequivocally is associated with differential liabilities by various drugs belonging to both first generation and second generation groups. Among the first generation, the phenothiazine group like chlorpromazine has more risk than high potency butyrophenones like haloperidol. After the introduction of second generation antipsychotics, it was found that they cause more metabolic derangements than first generation antipsychotics by various studies. Clozapine and olanzapine causes more derangements, risperidone and quitiapine to the moderate extent.ziprazidone, aripiprazole has doubtful liabilities. The current study is one of few studies done in first episode drug naive persons to eliminate the disease effect and very few studies were done in these populations.

At the end of two months in metabolic derangements, there are no differences among educational status, marietal states, religion, and occupation.Out of 10 persons who developed metabolic syndrome, 7 persons had illness duration less than 1 year. sedentary lifestyle pattern was seen in 8 persons and positive family history of metabolic diseases in 7 persons. Early response to anti psychotics with more than 40% reduction as seen in PANSS score, was positively associated with weight gain, rise in fasting plasma glucose, increases in triglycerides, decreases in HDL cholesterol significantly(

p value .002). This pattern was reported earlier by Lane et al 2003. The correlation of glucose regulation with rise in body mass index may be secondary to adiposity. -Eder et al 2001. This may contribute to 30 to 40% of variance of insulin resistence-Farin et al 2005. At the same time a significant population develop insulin resistence independent of it-Koller et al 2003. Risperidone had minimal propensity to increase waist circumference rather than hip circumference without significant difference between the groups(p .202) in overall increases in body mass index. In both systolic and diastolic blood pressure, there was reduction in risperidone group(mean score 9.37) with high significant p value of .000 as against rise in haloperidol group(mean rise 7). This may be explained by the risperidone's significant action at alpha-2 adrenergic receptors. No persons met the criteria for metabolic syndrome during the first two months. All other parameters of metabolic components correlated with the later development of metabolic syndrome as shown in earlier studies.

At the end of four months, the differences in blood pressure change is significant (p.000) between the groups with rise in both groups 7.14 in risperidone and 2 in haloperidol and the overall change is insignificant (p .064) .Two persons in haloperidol (8.3%) and 3 persons (10.3%) in risperidone group developed metabolic syndrome.

At the end of six months 10 persons (18.86%) developed metabolic syndrome as per the US national cholesterol education treatment programme

(Adult treatment panel III) criteria. Haloperidol group caused 4 persons (16.6%) and risperidone group caused 6 persons (20.6%) with minimal increases in the risperidone group, which was found to be statistically insignificant.The minimal difference in producing metabolic changes between risperidone and haloperidol was shown in various studies like one conducted by Saddichsa, Manchunatha, a short term prospective study (6 weeks duration).The changes in blood glucose level occurred in 9.1% in risperidone and 9.7% in haloperidol group. This study was conducted in Indian population. A similar Indian study done by Shiv Gautham,Parth sing Meena in drug naive schizophrenia, which is a randomized prospective study done for 4 months showed 11.66% metabolic syndrome after 4 months. No patient met criteria for metabolic syndrome with haloperidol, with minimal changes and 10% in the risperidone group developed metabolic syndrome. A meta-analysis done by Goodnig anbGerry 2002 showed less difference among haloperidol and risperidone to produce dyslipidemia. A prospective study in Indian population revealed no significant changes in the end among Trifluperazine, haloperidol, and olanzapine for BMI and glycemic changes. A similar study by Babes J et al in schizophrenia showed weight gain in 30.6% for risperidone and22.4% for haloperidol.

CONCLUSION

Antipsychotic drug both risperidone and haloperidol causes significant rise in weight, body mass index, plasma glucose, triglycerides, HDL cholesterol, hip circumference, waist circumference. Risperidone has slight preference to elevate waist circumference rather than hip circumference compared with haloperidol. The changes were more marked during the first two months. This shows the need for stringent guide lines in antipsychotic treatment to prevent the cardiovascular and cerebrovascular morbidity and mortality. In contrast to other metabolic derangements, risperidone causes reduction in blood pressure changes, more so during the first two months as against the gradual rise in haloperidol with the therapeutic implication of precaution at the initiation of the drug. The absence of significant difference between the two groups show, among the second generations, risperidone may be considered as equivalent to haloperidol for changes in metabolic profile except reduction in blood pressure, which is most significant disadvantage. The blood pressure lowering effect of risperidone is more marked during the earlier months with the continuing effect in this study warrants stringent precautions to avoid potential complications.

LIMITATIONS

* Inadequate sample size (24 in haloperidol and 29 in risperidone group) may have limitations in the result.

* The pattern of diet intake,apart from the physical activity has to be considered in detail in future studies.

* The duration of study of 6 months may not be adequate to unravel the metabolic derangements.

FUTURE IMPLICATIONS

* More studies have to be conducted in drug naive persons as there are limited ones in this area especially in Indian contexts.

* Exploration in the pharmacogenomic research is a promising area to have the drugs with limited side effects in future.

* Primary prevention in the form of modification of lifestyle pattern has to be emphasized apart from at the secondary and tertiary level.

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ANNEXURE

1. American heart association- [An update of NCEP III] criteria. (Any 3 of the following 5 items) criteria for metadolicsyndrome.

- Waist circumference more than 40 inches [102cms] for male and 35 inches [88cms] for female.
- TG 150mgs or more [1.7mmol/lit].
- HDL 40 or more [1.03mmol/lit] for male and 50 0r more [1.29mmol/lit] for female.
- BP 130/85 or medication in the past.
- Fasting plasma glucose of 100mgms% [5.6mmol/lit] or treatment in the past.

Others

- High 'C'reactive protein used as marker to predict coronary vascular disease in metabolic syndrome and it was recently used as a predictor for non-alcoholic fatty liver disease in correlation with serum markers that indicated lipid glucose metabolism.

2. POSITIVE AND NEGATIVE SYNDROME SCALE. [PANSS]

Positive and negative syndrome scale was developed specifically to address the psychometric limitations. It is more comprehensive, strictly operationalized and standardized. Assessment is done in four phases 35-45 minutes clinical interview. (KAY, FISZBEIN, OPLER 1987, AND KAY, OPLERLINDENMAYER 1988, 1989].

Phase -1. First non directive 5-10 minutes interview to establish rapport. Phase 2- semi structured phase lasting for 15-20 minutes to elucidate from the non-directive phase, the questions ranging from unspecific to specific, direct queries. Phase 3-structured phase lasting for another 5-10 minutes for more focused and often with varied and rotated ones during repeated assessment. Phase 4-Final directive phase to probe ambivalent, guarded response lasting for another 5-10 minutes.

It contains seven items scores for each positive and negative syndrome, 16 items for general psychopathology, which is scored on seven point

severity.1 denotes absence of symptom, 2 minimal or suspected, 3 for clearly established and interferes little in day-to-day functioning,4 for moderate level occasionally interferes in functioning, 5 for moderately severe, distinctively impact but not all consuming, 6 severe for gross pathology requiring supervision, 7 extreme drastic interference requiring close supervision. Scores are categorised separately and as total scores in terms of raw, percentile and range.

POSITIVE SCALE

P1 -delusion

P2 -conceptual disorganization

P3 -hallucinatory behaviour

P4 -excitement

P5 -grandiosity

P6 -suspiciousness

P7 -hostility

Negative scale

N1 –blunted affect

N2 -emotional withdrawal

N3 -poor rapport

N4 -passive/apathetic social withdrawal

N5 -difficulty in abstract thinking

N6 -lack of spontaneity and flow of conversation

N7 -stereotyped thinking

General psychopathology scale

G1 -somatic concern

G2 -anxiety

G3 -guilt feeling

G4 -tension

G5 -mannerism and posturing

G6 -depression

G7 -motor retardation

G8 -uncooperativeness

G9 -unusual thought content

G10 -disorientation

G11 -poor attention

G12 -lack of judgement and insight

G14 -disturbance of volition

G15 -poor impulse control

G16 -active social avoidance

Positive syndrome -sum of P1through P7

Negative syndrome -sum of N1 through N7

General psychopathology –sum of G1 through G16

Composite index -positive syndrome-negative syndrome

Anergia -N1+N2+G7+G10

Thought disturbance

Activation

Paranoid / belligerence

Depression

Positive Syndrome	-	Sum of P1 through P7
Negative Syndrome	-	Sum of N1 through N7
Composite index Syndrome	-	Positive Syndrome minus Negative
General Psychopathology	-	Sum of G1 though G16
Anergia	-	N1+N2+N7+G10
Thought disturbance	-	P2+P3+P5+G9
Activation	-	P4+P3+P5+G9
Paranoid / belligerence	-	G1+G2+G3+G6

3. SIMPSON ANGUS SCALE (SAS)

The Simpson Angus Scale (extra pyramidal Side Effects Rating Scale) is a 10-item instrument developed by GM Simpson and JW Angus.It measures the parkinsonian side effects of rigidity, tremor, akinesia, and salivation.

The 10 items are present on a five- point scale (0= complete absence of the condition, 4 = presence of the condition of extreme form). 7 items measure rigidity and one item (gait) for akinesia. The global score is obtained by adding the total scores divided by the total number of items.Normal range is up to o.3 This is commonly used to find the side effects of antipsychotic medications. The mean correlation coefficients range from 0.87 for glabellar tap to 0.52 for gait. The inter ratter reliability is 0.71 to 0.96 -Friedman JH and Factor SA, "Atypical Antipsychotics in the Treatment of Drug- Induced Psychosis in Parkinson's Disease," Movement Disorder, 2000 15 (2)-201-11.

1. GAIT

The patient is examined for his gait, armswing, general posture.

0	=	Normal
1	=	Diminution in swing during walking
2	=	Marked diminution in swing with rigidity in the arm

3 = Stiff gait and arms held rigidly before the abdomen

4 = shuffling gait with propulsion and retropulsion.

2. ARM DROPPING

The patient and the examiner raise their arms to shoulder height and let them fall to their sides. A stout slap is normallyheard and with Parkinson's syndrome, the arms fall slowly.

0 = Normal with loud slap and rebound

1 = Slow fall and little rebound

2 = Fall slowed, no rebound

3 = Marked slowing, no slap.

4 = Arms fall as though against resistance.

3. SHOULDER SHAKING

The patients arms are bent at a right angle at the elbow and taken one at a time. The examiner who grabs one hand also clasps the other around the patient's elbow. The patients upper arm is manipulated to and from and the humerus is externally rotated. The degree of resistance scored.

0 = Normal

1 = Slight stiffness.

2 = Moderate stiffness.

3 = Marked rigidity.

4 = Extreme, with almost a frozen shoulder

4. ELBOW RIGIDITY

The elbow is separately bent at right angles and are passively extended and flexed.The biceps is observed and palpated and the resistance is rated of((cogwheel rigidity is noted separately).

0 = Normal

1 = Slight stiffness.

2 = Moderate stiffnes.

3 = Marked rigidity.

4 = Extreme stiffness with almost a frozen shoulder.

5. FIXATION OF POSITION OR WRIST

The wrist is held in one hand and then the fingers held by the examiner's other hand with the wrist moved to extension with ulnar and radial deviation.

0 = Normal

1 = Slight stiffness.

2 = Moderate stiffness.

3 = Marked rigidity.

4 = Extreme stiffness with almost a frozen shoulder.

6. LEG PENDULOUSNESS

The person sits on a table with legs hanging down and swinging free. The ankle is grasped and raised to partial extension and allowed to fall.

0 = The legs swing freely

1 = Slight diminution in the swing.

2 = Moderate resistance.

3 = Marked resistance.

4 = Complete absence of swing.

7. HEAD DROPPING

The patient lies on a well-padded table and the head is raised with the hand. The hand is withdrawn and the head is allowed to drop.Normally , the head will drop on the table. The delay or absence is noted.

0 = The head falls with a good thump.

1 = Slight slowing in fall.

2 = Moderate slowing.

3 = Falls stiffly and slowly

4 = Head does not reach table

8. GLABELLA TAP

Patient is told to open eyes and not blink. The glabellar region is tapped at a steady, rapid speed. The number of blinks is observed.

0 = 0-5 blinks

1 = 6-10 blinks

2 = 11-15 blinks

3 = 16-20 blinks

4 = 21 and more blinks

9. TREMOR

Person is observed first, then examined.

0 = Normal

1 = Mild tremor.

2 = Tremor occurring spasmodically

3 = Persistent tremor of one or more limbs

4 = Whole body tremor

10. SALIVATION

This is observed while talking and on opening the mouth.

0 = Normal

1 = Excess salivation on mouth opening.

2 = When excess salivation causing difficulty in speaking.

3 = Speaking with difficulty due to excess salivation.

4 = Frank drooling.

4. DSM IV-TR - Diagnostic criteria for schizophrenia

A. characteristic symptoms; two or more of the following, each present for a significant period of time during a 1 month period or less if successfully treated;

1. Delusions.

2 Hallucinaions

3. Disorganised speech [frequent derailment or incoherence]

4. Grossly disorganized or catatonic behavior

5. Negative symptoms like affective flattening, alogia or avolition.

Only one criterion A symptom is required if delusions are bizarre or hallucination of voice keeping a running commentary or voices conversing with each other.

B.social /occupational functioning-For a significant portion of time one or more areas of functioning like work, interpersonal relations or self care are markedly below normal or failure of expected development in case of children or adolescence.

C. Duration-continuous signs of disturbance persist for at least 6 months, including at least one month period of active symptoms or less if successfully treated including prodromal or residual period.

D.schizoaffective/mood disorder exclusion- no major depressive, manic or mixed episode concurrently with the active phase symptoms except for a brief period.

E.substance /general medical condition exclusion-the disturbance is not due to direct effect of general medical condition or substance abuse.

F.pervasive development disorder-additional diagnosis of schizophrenia is made if there are prominent delusions or hallucinations for at least one month if there is history of pervasive developmental disorders.

5. SCREENING PROFORMA

Case number Enrolment Date

Address

Informants

Identity marks

Date of visits

Educational status

Occupation

Marietal status

Religion

Language spoken

Socio-economic status-Low/Middle/High

Life style- sedentary/Active work/Strenuous work

Family history of first degree relatives

- Psychiatric disorder.
- Substance abuse/dependence.
- Chronic medical illness.

- Diabetes mellitus.
- Systemic hypertension.
- Dyslipidemia.
- Obesity

	Base line	**Two months**	**Four month**	**Six months**
• PANSS score • Simpson Angus score • Height • Weight • Waist circumference • Hip circumference • Body Mass Index • Blood sugar fasting and post prandial • Blood pressure • Triglycerides • HDL cholesterol • Drug name • Drug dose • Adverse reactions if any				

A COMPARATIVE STUDY BETWEEN FIRST GENERATION AND SECOND GENERATION ANTIPSYCHOTICS OVER THE DEVELOPMENT OF METABOLIC SYNDROME IN FIRST EPISODE DRUG NAIVE PERSONS WITH SCHIZOPHRENIA.

Introduction Metabolic syndrome denotes a constellation glycemic dysregulation, hypertension, dyslipidemia, elevated body mass index producing hypercoagulable and proinflmmatory state. Antipsychotics especially, second generation drugs cause more derangements. It occurs in schizophrenia which itself is a vulnerable factor.

Aim To compare the development of metabolic syndrome between these groups in drug naive first episode schizophrenia.

Method This is a randomized, prospective one .Risperdone had 29 and haloperidol 24 persons.They were assessed at baseline, second, fourth and six months.

Result Significant changes [p.000] occurred in elevation of body mass index, serum triglycerides, plasma glucose, and HDL cholesterol. This correlated with reduction in PANSS score, more so in the first two months, without significant inter group differences statistically. The risperidone group caused significant reduction in both systolic and diastolic blood pressure (p .006) as against gradual rise in haloperidol group, more marked in first two months.

Discussion The current study is one of very few studies done in drug naive first episode. over all 18.86% developed metabolic syndrome according to American heart association criteria, 20.6% in risperidone and 16.6% in haloperidol without significance statistically.This pattern of moderate potential of risperidone among second generation antipsychotics and the relatively low incidence of high potent haloperidol were shown in various studies.Risperidone's reduction reveals the therapeutic implication of stringent precaution on initiation of therapy.These inferences may be replicated in future with more samples and longer duration.